ACUTE TOXICITY SUMMARY

PHENOL

(carbolic acid, phenylic acid, phenyl hydroxide)

CAS Registry Number: 108-95-2

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level	**5,800 μg/m³**
Critical effect(s)	irritation of the eyes, nose, and throat
Hazard Index target(s)	Eyes; Respiratory System

II. Physical and Chemical Properties (HSDB, 1993 except as noted)

Description	colorless to light pink liquid
Molecular formula	C_6H_5OH
Molecular weight	94.11
Density	1.0576 g/cm^3 @ 20°C
Boiling point	181.75°C
Melting point	43° C
Vapor pressure	0.3513 mm Hg @ 25°C
Flashpoint	79°C (closed cup)
Explosive limits	upper = 8.6% (AIHA, 1992) lower = 1.7% (AIHA, 1992)
Solubility	very soluble in alcohol, carbon tetrachloride, acetic acid and liquid sulfur dioxide; soluble in chloroform, ethyl ether, carbon disulfide; slightly soluble in water and benzene
Odor threshold	0.060 ppm (geometric mean) (AIHA, 1989)
Odor description	medicinal, acid (AIHA, 1989)
Metabolites	o,p-hydroxylated products
Conversion factor	1 ppm = 3.85 mg/m³ @ 25°C

III. Major Uses or Sources

Phenol is obtained from coal tar and is widely used as a disinfectant for industrial and medical applications. It also serves as a chemical intermediate for phenolic resins and as a solvent for petroleum refining (HazardText, 1993). Approximately half of the US consumption is directly related to the housing and construction industries in applications such as germicidal paints and slimicides (HSDB, 1993).

IV. Acute Toxicity to Humans

Respiratory distress, pulmonary edema, cyanosis, muscular weakness, and loss of consciousness may be observed following inhalation exposure to phenol (Clayton and Clayton, 1982). Rapidly absorbed through the skin, phenol is corrosive and burns any tissue with which it comes in contact (Clayton and Clayton, 1982). Symptoms of acute phenol poisoning include headache, dizziness, photophobia, weakness, and difficulty breathing. Death from phenol poisoning is usually due to respiratory failure (Clayton and Clayton, 1982). It has been reported that ingestion of 4.8 g of pure phenol caused death within 10 minutes (HSDB, 1993). Ingestion may cause oral mucosal burns, nausea, vomiting, and severe abdominal pain. About 50% of the cases of acute overexposure to phenol are fatal (HSDB, 1993). The oral LD_{Lo} for adults is 14 g/kg with effects consisting of behavioral changes and cyanosis in addition to the previously described signs.

In a study designed to evaluate the absorption of phenol in the lungs and through the skin, eight volunteers were exposed either by face mask only or by skin only (accomplished by the use of a protective respirator) to up to 6.5 ppm phenol for 8 hours and their urinary excretion of phenol subsequently measured (Piotrowksi, 1971). The concentrations of phenol to which the volunteers were exposed by face mask only were approximately 1.6-5.2 ppm. The exposures included two 30-minute breaks commencing at 2.5 and 5.5 hours after the start of exposure. The intent of this study was to determine whether urinary excretion of phenol could serve as an adequate biomarker of dermal and inhalation exposure. No mention of adverse effects in the volunteers was made. Therefore, a free-standing 8-hour NOAEL of 5.2 ppm can be determined from this study. A human irritancy threshold for phenol of 182.4 mg/m³ (47 ppm) was reported by Ruth (1986).

Predisposing Conditions for Phenol Toxicity

Medical: Individuals with skin, eye, respiratory, hepatic or renal diseases may be more susceptible to the toxic effects of phenol (Clayton and Clayton, 1982).

Chemical: Unknown

V. Acute Toxicity to Laboratory Animals

The inhalation LC_{50} values for an unspecified duration of exposure in rats and mice are reported as 316 mg/m³ (82 ppm) and 177 mg/m³ (46 ppm), respectively (RTECS, 1993). Smyth (1956) reported that rats survived an 8-hour inhalation exposure to saturated phenol vapors (approximately 323 ppm at 25ºC).

A 5-minute RD_{50} of 166 ppm was observed in mice (DeCeaurriz *et al*., 1981). Kane *et al*. (1979) report a predictable qualitative correlation between a reduction in rate of respiration in experimental animals (RD_{50}) exposed to airborne sensory irritants, and the symptoms observed in humans exposed to the same irritants.

Deichmann *et al*. (1944) observed that guinea pigs exposed to concentrations of phenol between 25 and 50 ppm (96 and 200 mg/m³) 7 hours per day, five days per week, for four weeks displayed

signs of respiratory difficulty and paralysis which affected primarily the hind quarters. Five of twelve animals exposed at this concentration died. At necropsy, extensive myocardial necrosis, lobular pneumonia, fatty degeneration of the liver, and hepatocellular necrosis were observed in all animals exposed at this level. Rabbits exposed at these same concentrations for 12 weeks did not exhibit any signs of discomfort, but showed similar findings at necropsy. No indications of toxicity were observed in rats during a 10-week exposure to the same concentrations. Necropsy findings in the rats were normal.

Based on data on species variation in the conjugation of phenol and its metabolite quinol, the metabolism of phenol by rats appears to be closer to that of humans than rabbits or guinea pigs. The percent glucuronide and sulphate conjugates of phenol and metabolite in test species administered phenol orally was compared to that of conjugates excreted by humans. The excretion of these conjugates by the rat was most similar to that observed in humans following phenol exposure (Capel *et al*., 1972a,b).

Groups of 10 monkeys, 50 rats, and 100 mice were exposed to 0 or 5 ppm phenol continuously for 90 days (Sandage, 1961). Hematological parameters and kidney function tests were normal. Additionally, the author reported no significant pathological findings at necropsy.

VI. Reproductive or Developmental Toxicity

No adverse fetotoxic or teratogenic effects were found following treatment of pregnant rats with an intraperitoneal injection of phenol during gestation days 8-10 or 11-13 with up to 200 mg/kg (Minor and Becker, 1971). In rats, radiolabeled phenol was found to equilibrate between the maternal and embryonic serum in equivalent levels (Gray and Kavlock, 1990).

A dose-related reduction in fetal weight was observed following oral administration of 30, 60, and 120 mg/kg/day phenol to pregnant rats on days 6-15 of gestation (Jones-Price *et al*., 1983). No teratogenic or fetotoxic effects were observed.

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects): 1.5 ppm (5.8 mg/m^3)

Study	Piotrowski, 1971
Study population	eight human volunteers
Exposure method	inhalation of phenol by face mask only
Critical effects	irritation of the eyes, nose, and throat
LOAEL	not determined in this study
NOAEL	5.2 ppm (free standing)
Exposure duration	8 hours
Extrapolated 1 hour concentration	15 ppm (5.2^2ppm * 8 h) = C^2 * 1 h) (see Table 12 for information on "n")
LOAEL uncertainty factor	1

Interspecies uncertainty factor	1
Intraspecies uncertainty factor	10
Cumulative uncertainty factor	10
Reference Exposure Level	1.5 ppm (5.8 mg/m³; 5,800 µg/m³)

No adverse effects were reported in 8 volunteers exposed to 5.2 ppm for 8 hours. The study was designed to quantify dermal and respiratory absorption of phenol and not to detect mild irritation, but it contains the best available human acute inhalation exposure data. The irritation threshold of 47 ppm reported by Ruth (1986) does not contradict the determination of an 8-hour NOAEL of 5.2 ppm from this study.

Level Protective Against Severe Adverse Effects

No recommendation is made due to the limitations of the database.

AIHA developed an ERPG-2 of 50 ppm (190 mg/m³) based on Flickinger (1976) where rats exposed for 8 hours to 900 mg/m³ (235 ppm) phenol exhibited tremors (Flickinger, 1976). After 4 hours, ocular and nasal irritation, loss of coordination, and muscular spasms were observed. However, the ERPG rationale incorrectly cites this study as reporting a 1-hour exposure of 312 ppm (1,200 mg/m³) in rats. The only acute inhalation exposure data included in the paper by Flickinger is exposure for 8 hours to 235 ppm as summarized above. No uncertainty factors or methods of extrapolating from a 4-hour exposure to an equivalent 1-hour exposure were reported by AIHA.

Level Protective Against Life-threatening Effects

No recommendation is made due to the limitations of the database.

AIHA developed an ERPG-3 of 200 ppm (770 mg/m³). Exposure of rats to 900 mg/m³ (235 ppm) phenol for four hours resulted in ocular and nasal irritation, slight loss of coordination and muscular spasms (Flickinger, 1976). The method used by AIHA (1992) for calculating the ERPG-3 value from the data was not reported. The rationale does include the observation that no reports of fatalities from inhalation have been reported in humans. No uncertainty factor is included for animal to human extrapolation.

NIOSH (1995) reports an IDLH of 250 ppm. It is based on animal inhalation toxicity data and on an analogy to cresol.

VIII. References

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